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R^1 is OH, $O(CH_2)_{1-2}OH$, OCH_2CO_2H , CO_2H , $[O-Z-C(O)NHCHR^8(CH_2)_{0-5}R^{17}]$

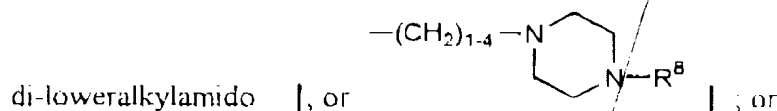
$O-Z-C(O)NH(CH_2)_{1-6}R^{17}$ or $[OCH_2-4-Phe-C(O)NHCHR^{18}(CH_2)_{0-5}R^{17}]$

$OCH_2-4-Phe-C(O)NH(CH_2)_{1-6}R^{17}$,

R^2 is H or lower alkyl;

R^3 is H, alkyl, aryl, or arylalkyl;

R^4 and R^5 are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido.



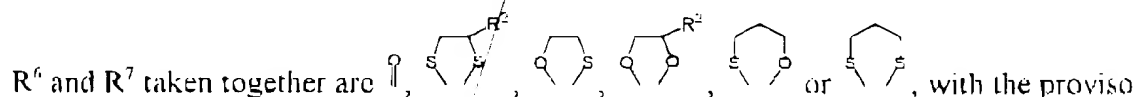
R^4 and R^5 taken together are $-(CH_2)_n-$, $-(CH_2)_2-O-(CH_2)_2-$,

$-CH_2-O-(CH_2)_3-$, $-(CH_2)_2-NR^6-(CH_2)_2-$, $-CH_2-NR^6-(CH_2)_m-$,

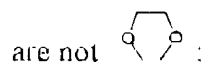
$[-(CH_2)_2XH(NHR^6)(CH_2)_2-]$ $[$ $-(CH_2)_2CH(NHR^6)(CH_2)_2-$ $]$,

$-(CH_2)_2-S(O)_{0-2}-(CH_2)_2-$, or $CH_2CH(N-loweralkyl)(CH_2)_2CHCH_2-$;

one of R^6 and R^7 is H and the other is H, OH, or $N(CH_2)_{1-6}R^{14}R^{15}$; or



that when R^1 is $-OH$ and R^2 is $-H$, R^6 and R^7 are not $-H$ and $-OH$ or when taken together



R^8 is H, $COOR^9$, $CONHR^{10}$, $CSNHR^{11}$, COR^{12} , SO_2R^{13} , lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN, NH_2 , $COOH$, $CONH_2$, carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or

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bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower alkyl, carboalkoxy, CONH₂, and S-lower alkyl;

R⁹ is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring wherein the hetero atom is O or N, wherein heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo,

R¹⁰ and R¹¹ are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;

R¹² is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S and - lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;

R¹³ is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;

R¹⁴ is H; [alkyl]; alkyl substituted by 1-3 alkoxy, [S-, loweralkyl] S-loweralkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl, -CH₂NR¹⁶C(O)R¹⁶; -C(O)NR¹⁶R¹⁶; -CH₂OC(O)R¹⁶; or -CH₂SC(O)R¹⁶;

R¹⁵ is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR³R³;

R¹⁶ is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R¹⁷ is H; [alkyl]; alkyl substituted by 1-3 alkoxy, [S-, loweralkyl] S-loweralkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl, substituted aryl;

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heteroaryl; substituted heteroaryl; heterocycloalkyl; [heterocycloalkyl; diphenylmethyl;]

$-\text{CH}_2\text{NR}^{16}\text{C}(\text{O})\text{R}^{16}$; $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{16}$; $-\text{CH}_2\text{OC}(\text{O})\text{R}^{16}$; or $-\text{CH}_2\text{SC}(\text{O})\text{R}^{16}$;

[R^{16} is H or $-(\text{CH}_2)_{0.5}\text{R}^{17}$];

X is alkyl, aryl, arylalkyl, O-loweralkyl, or $-\text{NR}^3\text{R}^1$;

Z is $-(\text{CH}_2)_{1-6}$, optionally substituted with 1-3 lower alkyl; $-\text{CHR}^2$; $-\text{Phe}-\text{CH}_2$ -, where Phe is optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene- (CH_2) -;

m is 2 or 3;

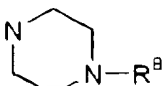
n is 4-9;

or a pharmaceutically acceptable salt thereof.

7. (once amended) A compound of claim 4 wherein:

R^1 is OH, $\text{OCH}_2\text{C}(\text{O})\text{NH}(\text{CH}_2)_{1-6}\text{R}^{17}$, or OCH_2 -4-Phe- $\text{C}(\text{O})\text{NH}(\text{CH}_2)_{1-6}\text{R}^{17}$;

[R^2 is H or lower alkyl;]

R^4 and R^5 are each lower alkyl [or $-(\text{CH}_2)_{1-4}-\text{N}$ ] ; or

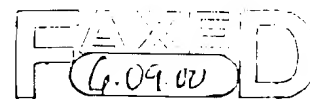
R^4 and R^5 taken together are $-(\text{CH}_2)_5$ -, $-(\text{CH}_2)_2\text{-O-}(\text{CH}_2)_2$ -,

$-(\text{CH}_2)_2\text{-NR}^8\text{-(CH}_2)_2$ -, $-(\text{CH}_2)_2\text{-CH(NHR}^8)(\text{CH}_2)_3$ -, $-(\text{CH}_2)_2\text{-S-(CH}_2)_2$ -,

or $\text{CH}_2\text{CH(NCH}_3)(\text{CH}_2)_2\text{CHCH}_2$ -;

R^6/R^7 are H/OH; $-\text{O}$ -, or $-\text{S}(\text{CH}_2)_2\text{-S-}$;

R^8 is H, COOR^9 , CONHR^{10} , CSNHR^{11} , COR^{12} , SO_2R^{13} , lower alkyl, aryl lower alkyl, heteroaryl wherein the ring members include 1 to 3 N atoms and the substituents are halo or amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;



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R^9 is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuranyl, tetrahydropyranyl, or aryl substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene dioxy, and halo;

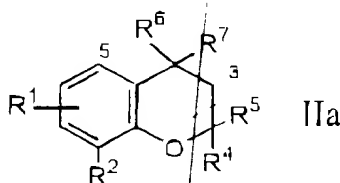
R^{10} and R^{11} are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

R^{12} is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl;

R^{13} is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

or a pharmaceutically acceptable salt thereof.

10. (once amended) A compound of claim 4 of the formula:



wherein:

R^1 is [6-or 7-OCH₂C(O)NHCHR¹⁸(CH₂)₀₋₅R¹⁷, 6-or 7-OCH₂-4-Phe-C(O)NHCHR¹⁸(CH₂)₀₋₅R¹⁷]

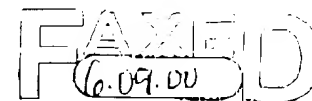
6- or 7-OCH₂C(O)NH(CH₂)₁₋₆R¹⁷ or 6- or 7-OCH₂-4-Phe-C(O)NH(CH₂)₁₋₆R¹⁷

when R^2 is H,

R^1 is [7-OCH₂C(O)NHCHR¹⁸(CH₂)₀₋₅R¹⁷, or 7-OCH₂-4-Phe-C(O)NHCHR¹⁸(CH₂)₀₋₅R¹⁷]

7-OCH₂C(O)NH(CH₂)₁₋₆R¹⁷ or 7-OCH₂-4-Phe-C(O)NH(CH₂)₁₋₆R¹⁷

when R^2 is CH₃;



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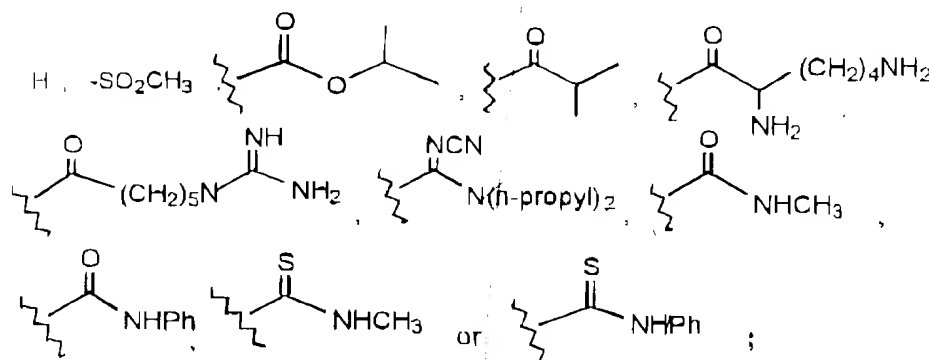
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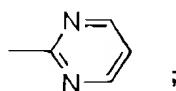
R^4 and R^5 are each methyl; or R^4 and R^5 taken together are $-(CH_2)_5-$, $-(CH_2)_2-O-(CH_2)_2-$,
 $-(CH_2)_2-NR^k-(CH_2)_2-$, $-(CH_2)_2-CH(NHR^k)(CH_2)_2-$, $-(CH_2)_2-S-(CH_2)_2-$, or
 $-CH_2CH(NCH_3)(CH_2)_2CHCH_2-$; or R^4 is methyl and R^5 is $-CH_2OCH_3$ or $-(CH_2)_3N(Et)_2$,

one of R^6 and R^7 is H and the other is OH; or R^6 and R^7 taken together are $=O$ or $-S(CH_2)_2S-$; or
 one of R^6 and R^7 is H and the other is NAB, where A is methyl, 2-methoxyethyl,
 2-phenylethyl, 4-methoxybenzyl, 2-tetrahydro-furanylmethyl,
 2-(3,4-dimethoxyphenyl)ethyl, or 2,2-diphenylethyl and

B is



R^k is H, $CONHCH_3$, SO_2Phe , $(CH_2)_3CH_3$, $CO(CH_2)_2CH_3$, benzyl, $C(O)-(4-Phe)-SO_2NH_2$, or



$(CH_2)_{1-6}R^{14}$ is methyl, n-butyl, 3-methoxy-n-propyl, CH_2 -c-propyl, or $-(CH_2)_{1-3}$ -phenyl, and
 $(CH_2)_{1-6}R^{17}$ is methyl, 2-methoxyethyl, 2-phenylethyl, 4-methoxybenzyl,
 methyl-2-tetrahydrofuranlyl, 2-(3,4-dimethoxyphenyl)ethyl, or 2,2-diphenylethyl;
 or a pharmaceutically acceptable salt thereof.

